

## PATENT COOPERATION TREATY

PCT

REC'D 07 JUN 2006

WIPO

PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

## (PCT Article 36 and Rule 70)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                 |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|----------------------|-----------------------------------------------|---------------------|------------------------------------------------|----------|--------------------------------------|--------------------------------------------------------------------------------------------------|-------------------------------------|----------------------------|-----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------------------|--------------------------------------|--------------------------------------------------|--------------------------------------------------|-------------------------------------------------------|
| Applicant's or agent's file reference<br>MJPahF598/79                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <b>FOR FURTHER ACTION</b>                                                                                                                                       |                                              | See Form PCT/PEA/416 |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| International application No.<br>PCT/EP2005/002882                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | International filing date (day/month/year)<br>04.03.2005                                                                                                        | Priority date (day/month/year)<br>05.03.2004 |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| International Patent Classification (IPC) or national classification and IPC<br>INV. A61K39/395 A61P29/00 A61P37/00                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                 |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| Applicant<br>INSTITUT NATIONAL DE LA SANTE ET DE LA ... et al.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                 |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> <i>(sent to the applicant and to the International Bureau)</i> a total of sheets, as follows:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</li> <li><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</li> </ul> <p>b. <input type="checkbox"/> <i>(sent to the International Bureau only)</i> a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> |                                                                                                                                                                 |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <p>4. This report contains indications relating to the following items:</p> <table> <tr> <td><input checked="" type="checkbox"/> Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input checked="" type="checkbox"/> Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/> Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/> Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/> Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/> Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/> Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/> Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                 |                                              |                      | <input checked="" type="checkbox"/> Box No. I | Basis of the report | <input checked="" type="checkbox"/> Box No. II | Priority | <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> Box No. VI | Certain documents cited | <input type="checkbox"/> Box No. VII | Certain defects in the international application | <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> Box No. I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Basis of the report                                                                                                                                             |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input checked="" type="checkbox"/> Box No. II                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Priority                                                                                                                                                        |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input type="checkbox"/> Box No. III                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input type="checkbox"/> Box No. IV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Lack of unity of invention                                                                                                                                      |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input checked="" type="checkbox"/> Box No. V                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input type="checkbox"/> Box No. VI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Certain documents cited                                                                                                                                         |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input type="checkbox"/> Box No. VII                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Certain defects in the international application                                                                                                                |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| <input checked="" type="checkbox"/> Box No. VIII                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Certain observations on the international application                                                                                                           |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| Date of submission of the demand<br>16.12.2005                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Date of completion of this report<br>06.06.2006                                                                                                                 |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |
| Name and mailing address of the international preliminary examining authority:<br><br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Authorized officer<br>Irion, A<br>Telephone No. +49 89 2399-8174                                                                                                |                                              |                      |                                               |                     |                                                |          |                                      |                                                                                                  |                                     |                            |                                               |                                                                                                                                                                 |                                     |                         |                                      |                                                  |                                                  |                                                       |



# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/EP2005/002882

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on
  - the international application in the language in which it was filed
  - a translation of the international application into , which is the language of a translation furnished for the purposes of:
    - international search (under Rules 12.3(a) and 23.1(b))
    - publication of the international application (under Rule 12.4(a))
    - international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements\*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

### Description, Pages

1-29 as originally filed

### Sequence listings part of the description, Pages

1-2 as originally filed

### Claims, Numbers

1-4 as originally filed

### Drawings, Sheets

1/8-8/8 as originally filed

- a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - the description, pages
  - the claims, Nos.
  - the drawings, sheets/figs
  - the sequence listing (*specify*):
  - any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/EP2005/002882

## Box No. II Priority

1.  This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
  - copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
  - translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2.  This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**see separate sheet**

## Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Yes: Claims |     |
|                               | No: Claims  | 1-4 |
| Inventive step (IS)           | Yes: Claims |     |
|                               | No: Claims  | 1-4 |
| Industrial applicability (IA) | Yes: Claims | 1-4 |
|                               | No: Claims  |     |

### 2. Citations and explanations (Rule 70.7):

**see separate sheet**

## Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2005/002882

**Supplemental Box relating to Sequence Listing**

**Continuation of Box I, item 2:**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
  - a. type of material:  
 a sequence listing  
 table(s) related to the sequence listing
  - b. format of material:  
 on paper  
 in electronic form
  - c. time of filing/furnishing:  
 contained in the international application as filed  
 filed together with the international application in electronic form  
 furnished subsequently to this Authority for the purposes of search and/or examination  
 received by this Authority as an amendment\* on
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.  
**PCT/EP2005/002882**

**Item II**

**II.1** The priority appears to be valid.

**Item V**

**V.1** The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: WO9941285 (MEDAREX INC.) 19 August 1999 (1999-08-19)

D2: US6018031 (L. SHEN & M.W. FANGER) 25 January 2000 (2000-01-25)

**V.2 Novelty (Article 33(2) PCT)**

**V.2.1 With respect to claims 1-4**

Document D1 describes the antibody A77 and the fragment scFv derived therefrom combined with a cytotoxic agent. Said conjugate is used to kill macrophages thereby inhibiting inflammatory reactions, such as observed in rheumatoid arthritis (p. 36 l. 15-17). Said antibody fragment may be further used for the treatment of autoimmune diseases such as diabetes mellitus, arthritis, SLE, asthma, allergic asthma and other cases of allergy such as atopic allergy (p. 48 l. 3-23). The antibody fragment is used to target the cytotoxic agent to the target cell, i.e the macrophage.

Document D2 describes the use of bifunctional antibodies comprising a binding region specific for Fc $\alpha$ R derived from the monoclonal antibody A77 (col. 4 l. 19-57) and the binding region of a target-specific antibody (abstract). Said target antigen derives from tumor cells, auto-antibody producing lymphocytes, or IgE producing cells in allergic diseases. Said bifunctional antibodies may be used for the treatment of autoimmune disorders such as diabetes mellitus, rheumatoid arthritis, SLE, Crohn's Disease, or allergies such as asthma (col. 16 l. 65 - col. 17 l. 50, col. 19 l. 66 - col. 20 l. 39). The antigen is targeted via the bifunctional antibody to effector cells of the immune system.

Therefore, the disclosure of each of D1 and D2 is novelty destroying for the subject-matter of claims 1-4. Therefore, claims 1-4 are not considered novel in the sense of

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.  
PCT/EP2005/002882

Article 33(2) PCT.

**V.3 Industrial applicability (Article 33(4) PCT)**

**V.3.1 With respect to claims 1-4**

The subject-matter of claims 1-4 appears to be susceptible of industrial application.

**Item VIII**

**VIII.1 With respect to claim 1**

The expressions "for treating an inflammatory disease" is vague and open to interpretation. Any infectious pathogen induces inflammatory reactions of the immune system or a cancer disease may include inflammatory activity, also. Furthermore, the expression "as anti-inflammatory active principle" is unclear. Therefore, said claim does not meet the requirements of Article 6 PCT.

**Further remark**

1. If claim 1 were limited to an unlabelled or unconjugated monovalent antibody fragment which is unambiguously distinguishable from the antibodies disclosed in D1 and D2 then said claim could be possibly considered novel.